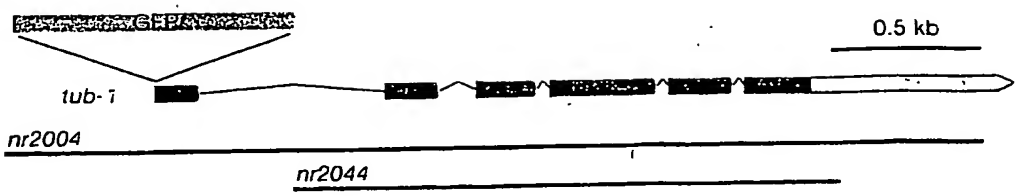
A



B

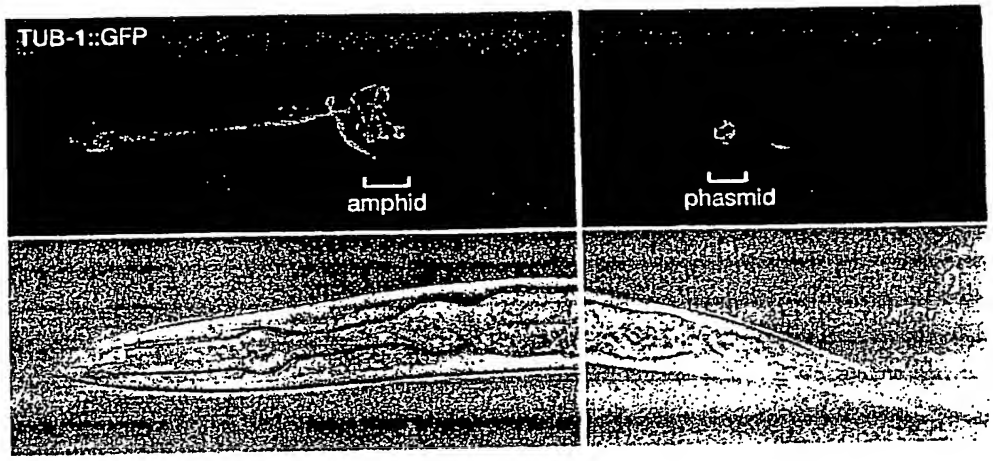
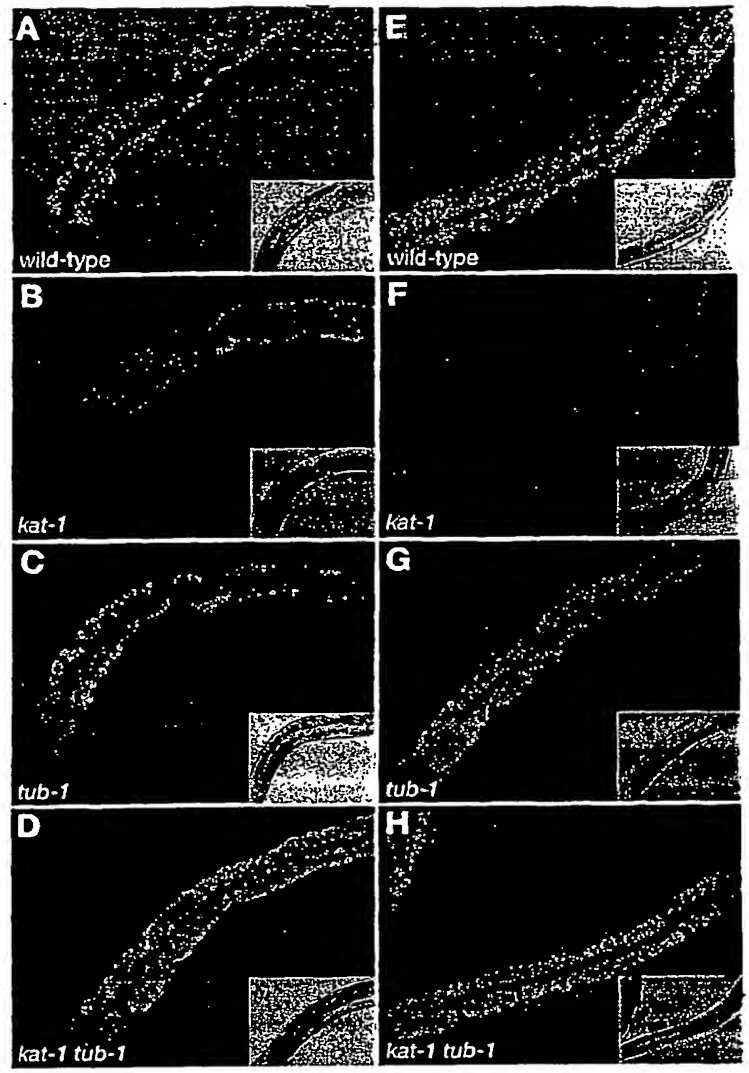


Figure 2


A
wild-type
B
kat-1
C
tub-1
D
kat-1 tub-1
E
wild-type
F
kat-1
G
tub-1
H
kat-1 tub-1

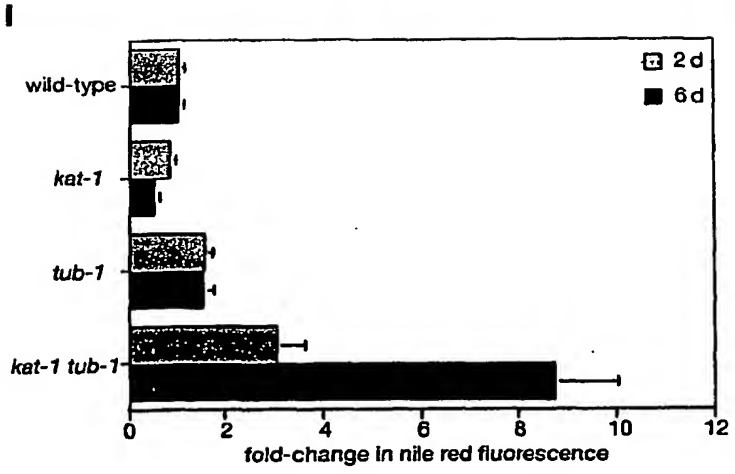

I
wild-type
kat-1
tub-1
kat-1 tub-1
2d
6d
0
2
4
6
8
10
12
fold-change in nile red fluorescence

Figure 3A

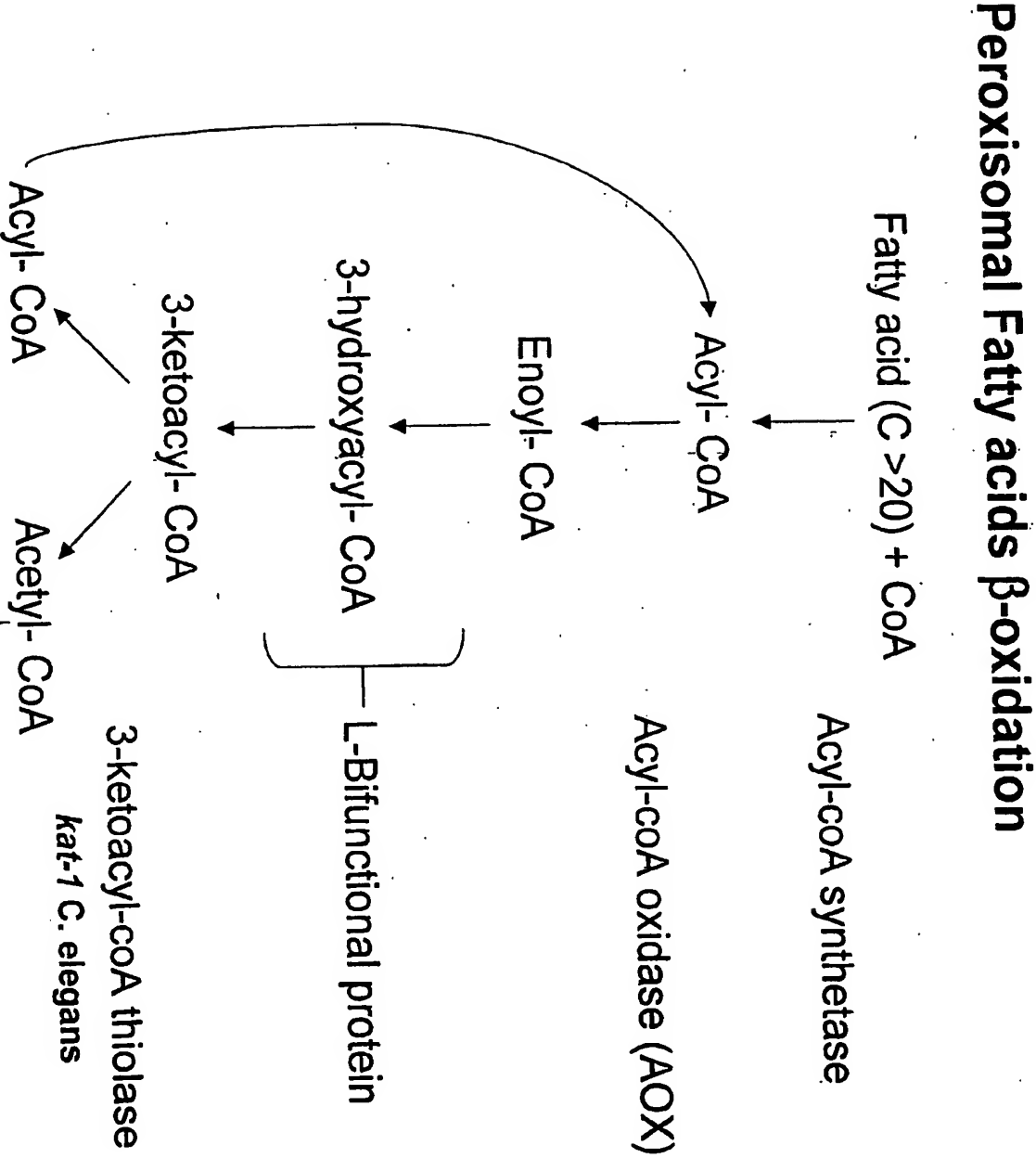
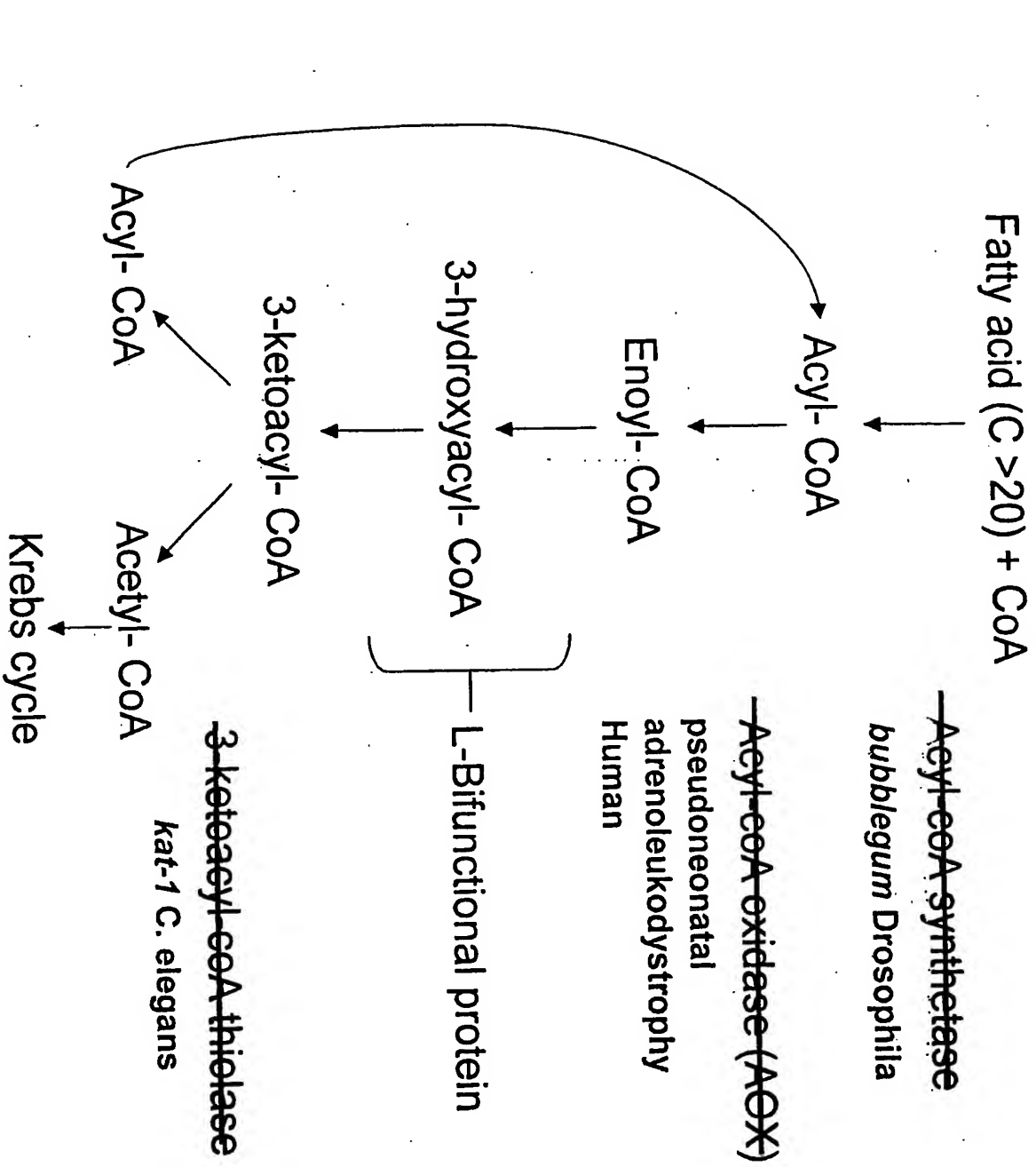

Peroxisomal Fatty acids β-oxidation
Fatty acid (C >20) + CoA
Acyl-coA synthetase
Acyl- CoA
Acyl-coA oxidase (AOX)
Enoyl- CoA
3-hydroxyacyl- CoA
L-Bifunctional protein
3-ketoacyl- CoA
3-ketoacyl-coA thiolase
kat-1 C. elegans
Acyl- CoA
Acetyl- CoA
Krebs cycle

Figure 3B


Peroxisomal Fatty acids β-oxidation
Fatty acid (C >20) + CoA
Acyl- CoA
Enoyl- CoA
3-hydroxyacyl- CoA
3-ketoacyl- CoA
Acyl- CoA
Acetyl- CoA
Krebs cycle
Acyl-coA synthetase
bubblegum Drosophila
Acyl-coA oxidase (AOX)
pseudoneonatal
adrenoleukodystrophy
Human
L-Bifunctional protein
3-ketoacyl-coA thiolase
kat-1 C. elegans

Sequence alignment of 3-ketoacyl-coA thiolase family members

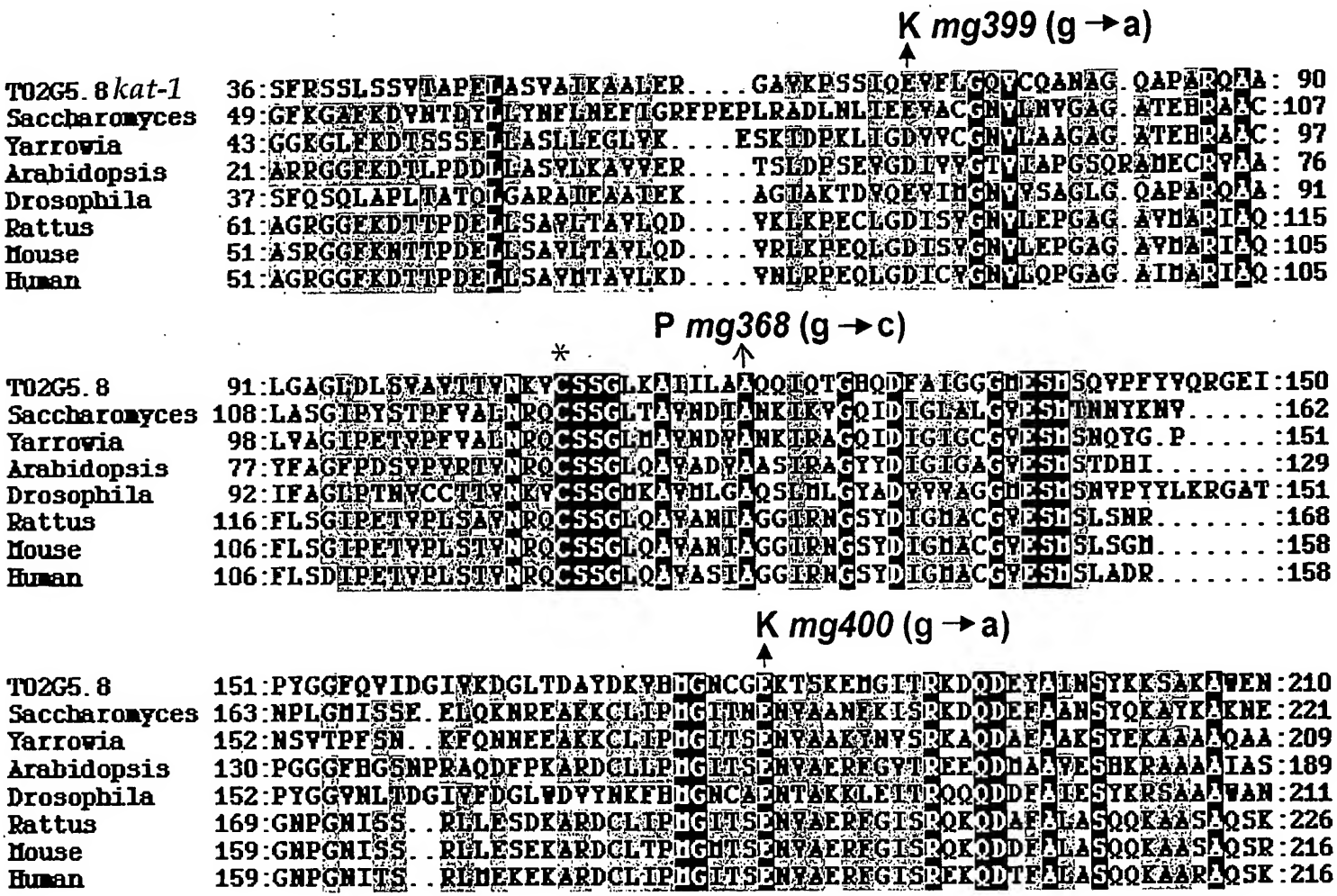


Figure 5

Sequence alignment of 3-ketoacyl-coA thiolase family members

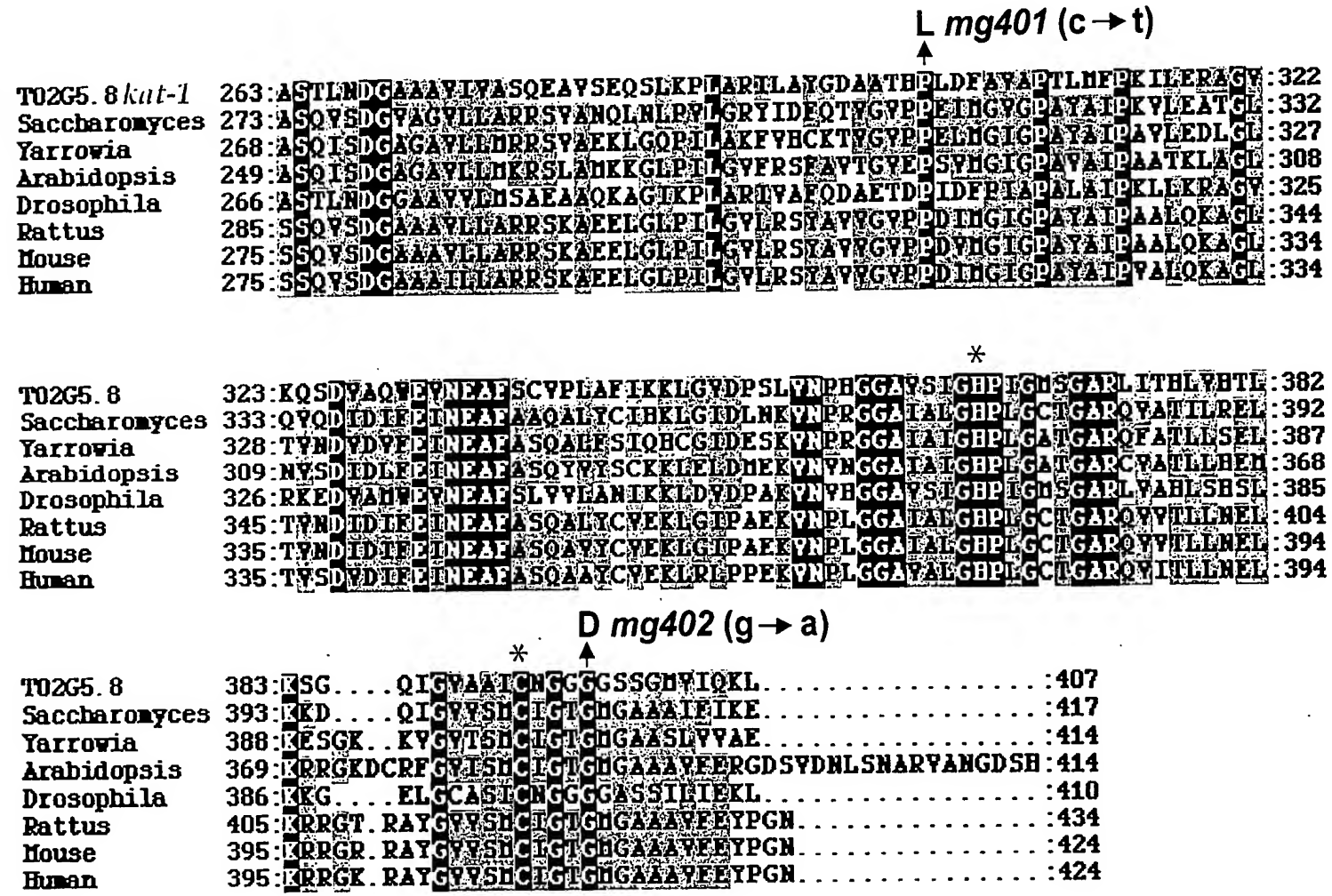


Figure 6

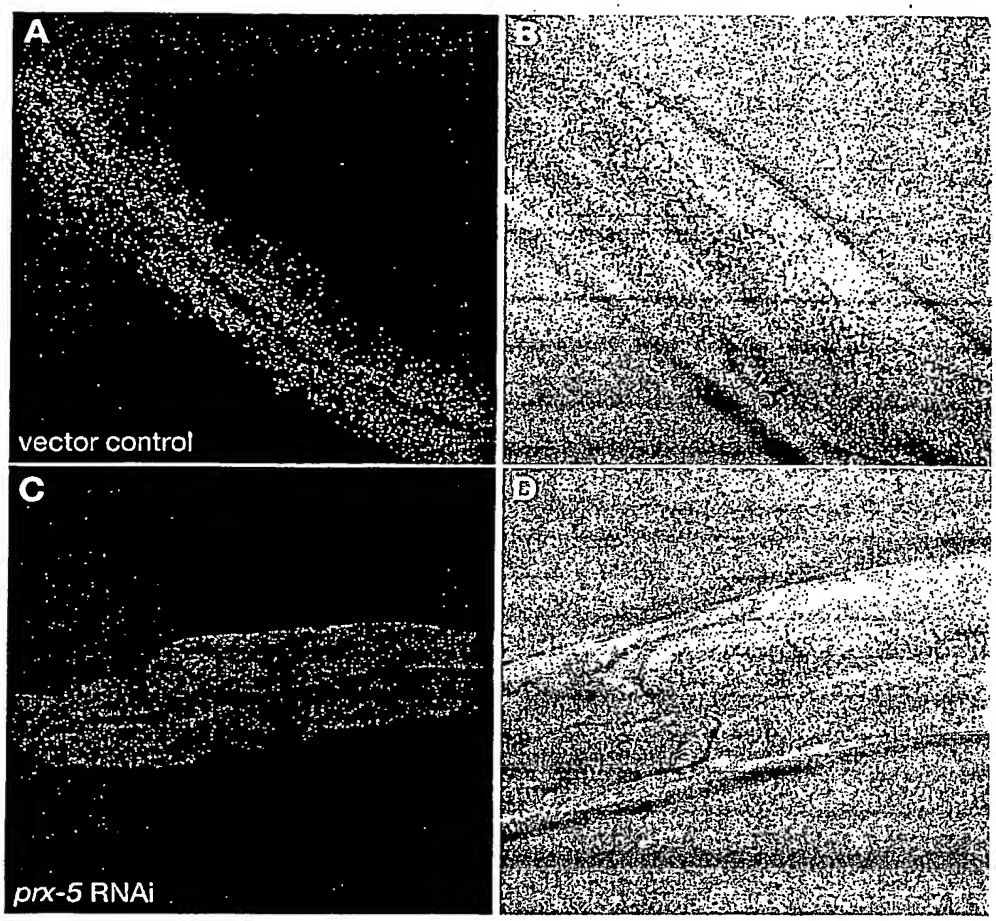


Figure 7A-7E

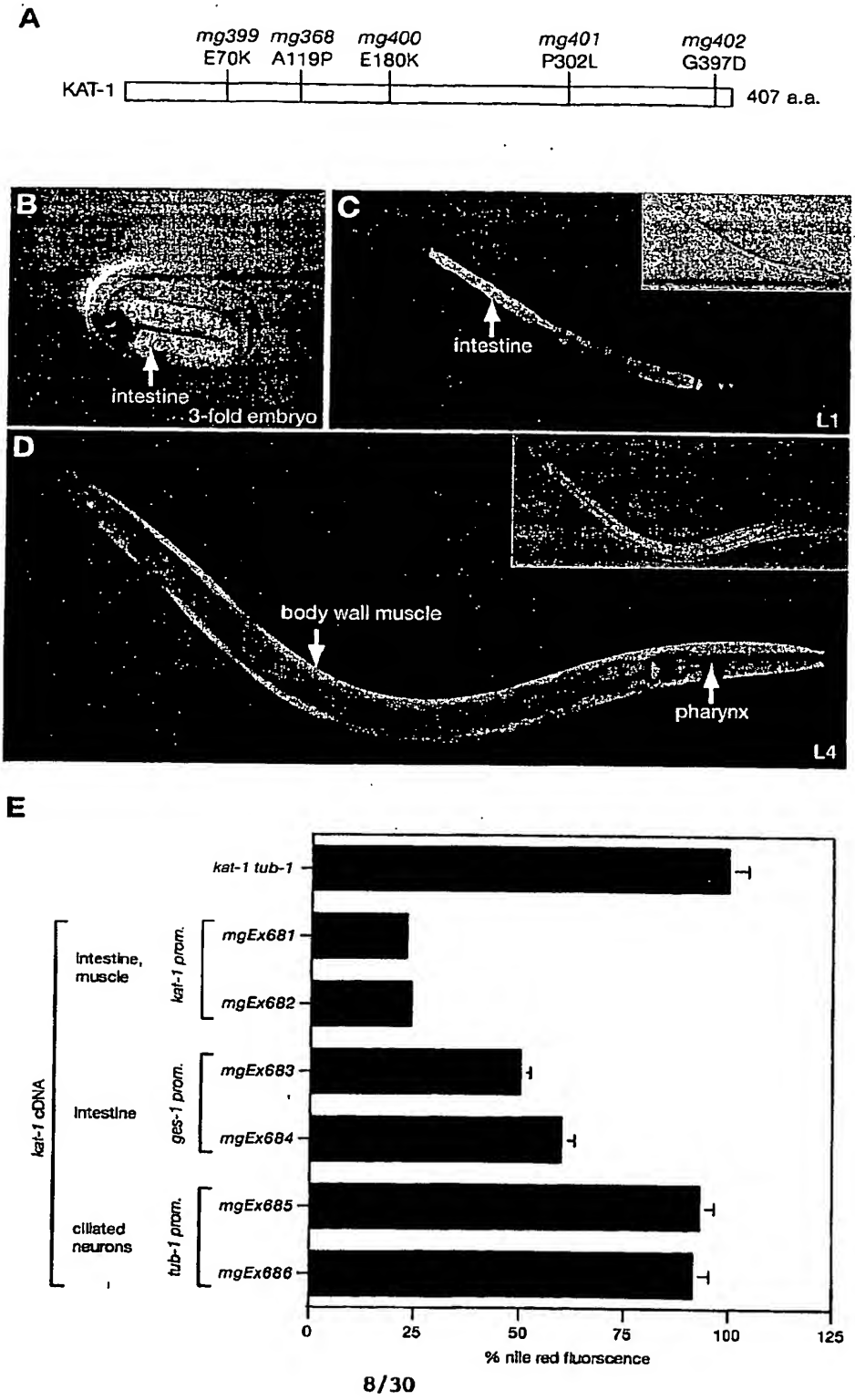

A
mg399 E70K
mg368 A119P
mg400 E180K
mg401 P302L
mg402 G397D
KAT-1
407 a.a.
B
intestine
3-fold embryo
C
intestine
L1
D
body wall muscle
pharynx
L4
E
kat-1 tub-1
kat-1 cDNA
Intestine, muscle
kat-1 prom.
mgEx681
mgEx682
Intestine
ges-1 prom.
mgEx683
mgEx684
ciliated neurons
tub-1 prom.
mgEx685
mgEx686
0
25
50
75
100
125
% nile red fluorscence

Figure 7F

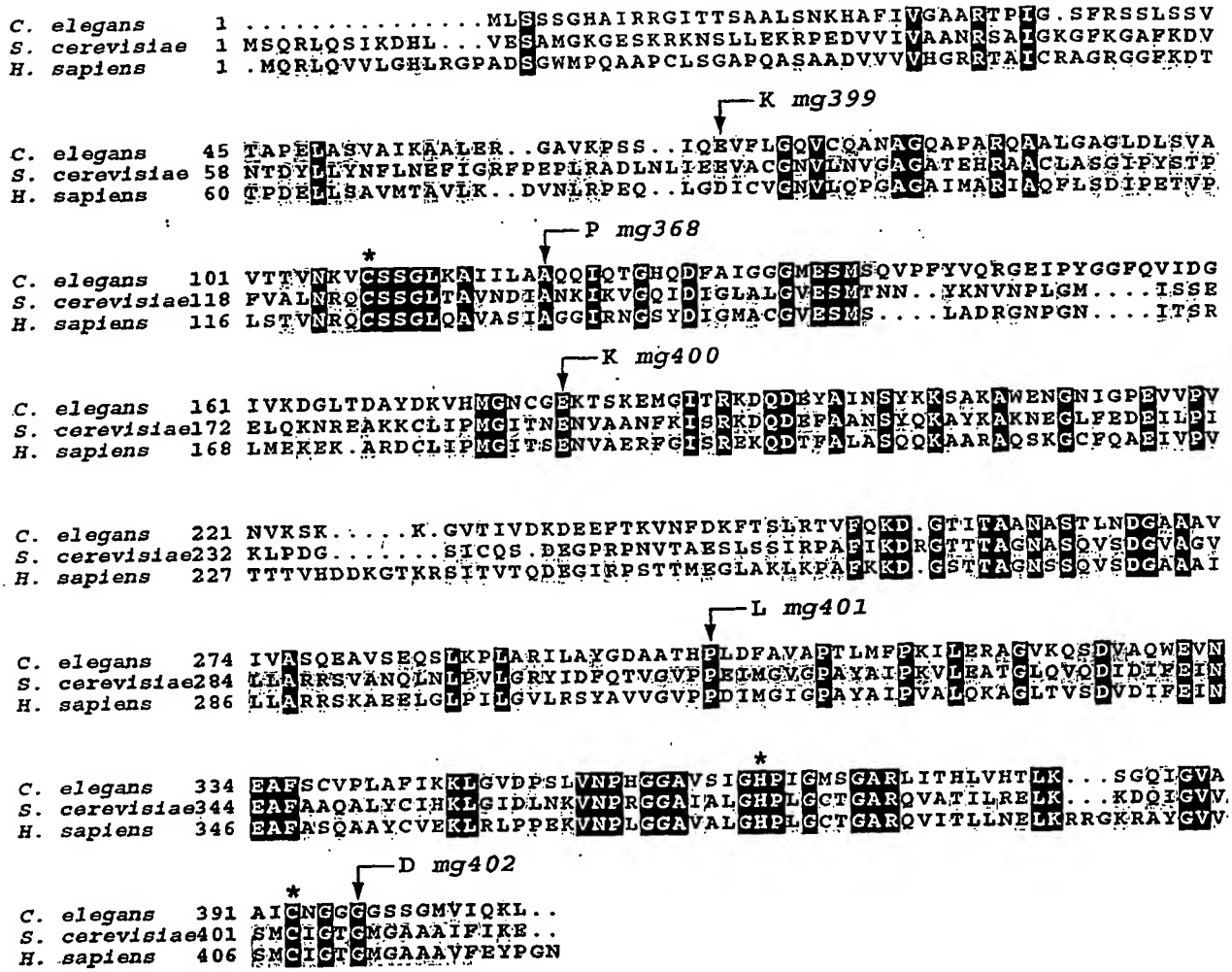
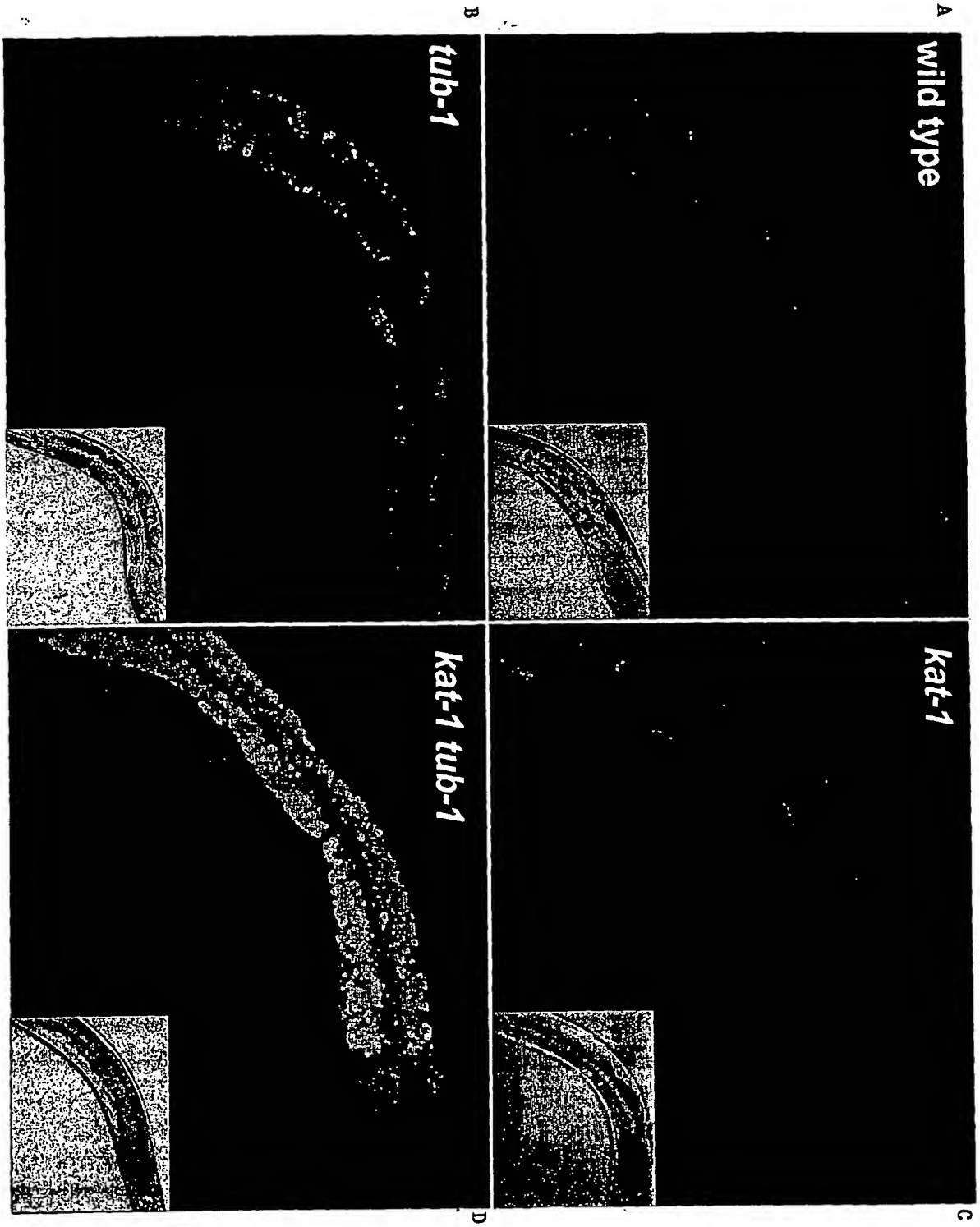

C. elegans 1 .....MLSSSGHAIRRGITTSAALSNKHAFIVGAARTPIG.SFRSSLSSV
S. cerevisiae 1 MSQRLQSIKDHL...VESAMGKGESKRKNSLLEKRPEDVVIVAANRSAIGKGFKGAFKDV
H. sapiens 1 .MQRLQVVLGHLRGPADSGWMPQAAPCLSGAPQASAADVVVVHGRRTAICRAGRGGFKDT
K mg399
C. elegans 45 TAPELASVAIKAALER..GAVKPSS..IQEVFLGQVCQANAGQAPARQAALGAGLDLSVA
S. cerevisiae 58 NTDYLLYNFLNEFIGRFPEPLRADLNLIEEVACGNVLNVGAGATEHRAACLASGIPYSTP
H. sapiens 60 TPDELLSAVMTAVLK..DVNLRPEQ..LGDICVGNVLQPGAGAIMARIAQFLSDIPETVP
P mg368
C. elegans 101 VTTVNKVCSSGLKAIILAAQQIQTGHQDFAIGGGMESMSQVPFYVQRGEIPYGGFQVIDG
S. cerevisiae 118 FVALNRQCSSGLTAVNDIANKIKVGQIDIGLALGVESMTNN..YKNVNPLGM....ISSE
H. sapiens 116 LSTVNRQCSSGLQAVASIAGGIRNGSYDIGMACGVESMS....LADRGNPGN....ITSR
K mg400
C. elegans 161 IVKDGLTDAYDKVHMGNCGEKTSKEMGITRKDQDEYAINSYKKSAKAWENGNIGPEVVPV
S. cerevisiae 172 ELQKNREAKKCLIPMGITNENVAANFKISRKDQDEFAANSYQKAYKAKNEGLFEDEILPI
H. sapiens 168 LMEKEK.ARDCLIPMGITSENVAERFGISREKQDTFALASQQKAARAQSKGCFQAEIVPV
C. elegans 221 NVKSK.....K.GVTIVDKDEEFTKVNFDKFTSLRTVFQKD.GTITAANASTLNDGAAAV
S. cerevisiae 232 KLPDG.....SICQS.DEGPRPNVTAESLSSIRPAFIKDRGTTTAGNASQVSDGVAGV
H. sapiens 227 TTTVHDDKGTKRSITVTQDEGIRPSTTMEGLAKLKPAFKKD.GSTTAGNSSQVSDGAAAI
L mg401
C. elegans 274 IVASQEAVSEQSLKPLARILAYGDAATHPLDFAVAPTLMFPKILERAGVKQSDVAQWEVN
S. cerevisiae 284 LLARRSVANQLNLEVLGRYIDFQTVGVPPELMGVGPAYAIPKVLEATGLQVQDIDIFEIN
H. sapiens 286 LLARRSKAEELGLPILGVLRSYAVVGVPPDIMGIGPAYAIPVALQKAGLTVSDVDIFEIN
C. elegans 334 EAFSCVPLAFIKKLGVDPSLVNPHGGAVSIGHPIGMSGARLITHLVHTLK...SGQIGVA
S. cerevisiae 344 EAFAAQALYCIHKLGIDLNKVNPRGGAIALGHPLGCTGARQVATILRELK...KDQIGVV
H. sapiens 346 EAFASQAAYCVEKLRLPPEKVNPLGGAVALGHPLGCTGARQVITLLNELKRRGKRAYGVV
D mg402
C. elegans 391 AICNGGGGSSGMVIQKL..
S. cerevisiae 401 SMCIGTGMGAAAIFIKE..
H. sapiens 406 SMCIGTGMGAAAVFEYPGN

Figure 8A-8D



Nile red staining of 2 day old adult

Figure 9

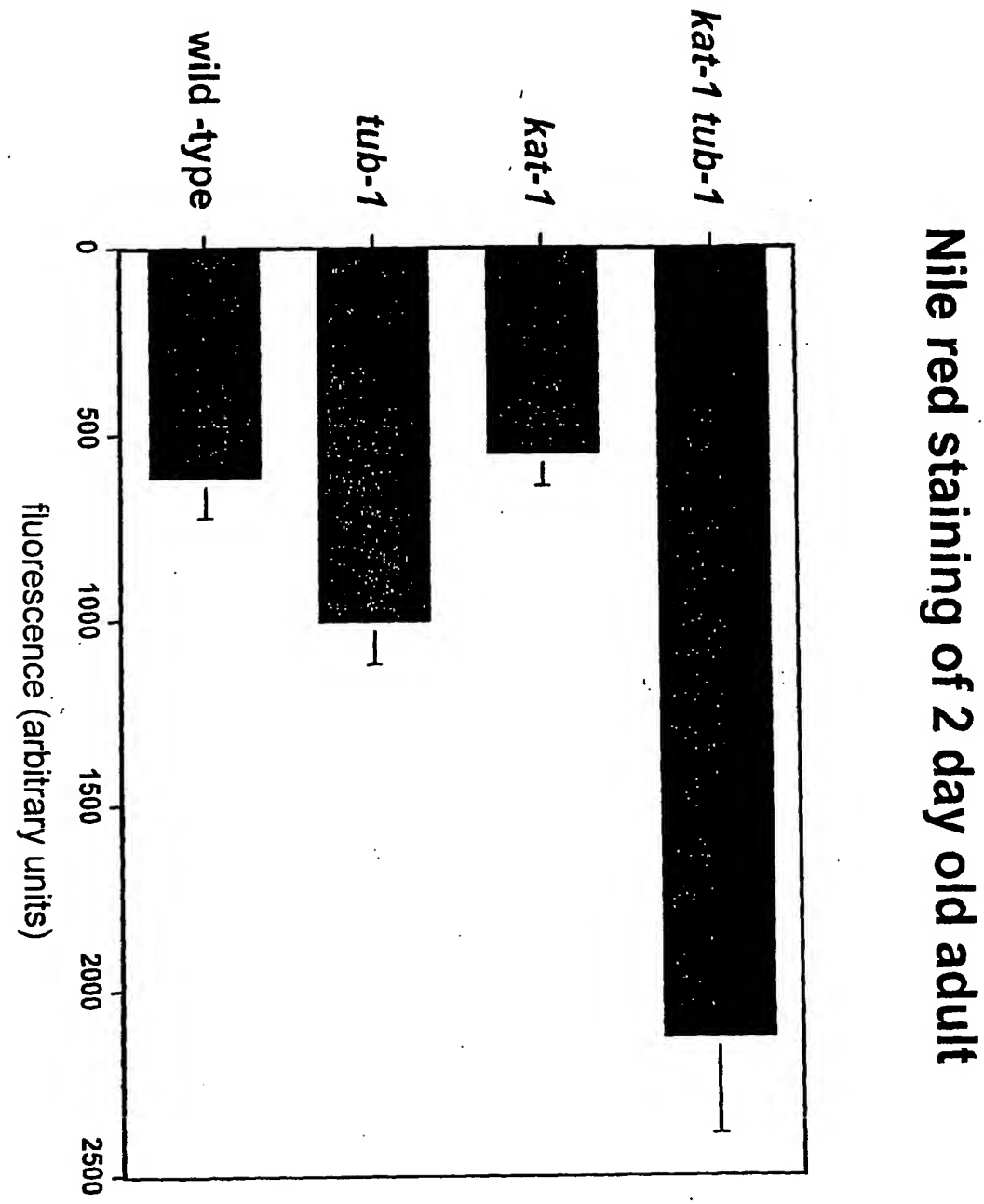

Nile red staining of 2 day old adult
wild -type
tub-1
kat-1
kat-1 tub-1
0
500
1000
1500
2000
2500
fluorescence (arbitrary units)

Figure 10A–10D

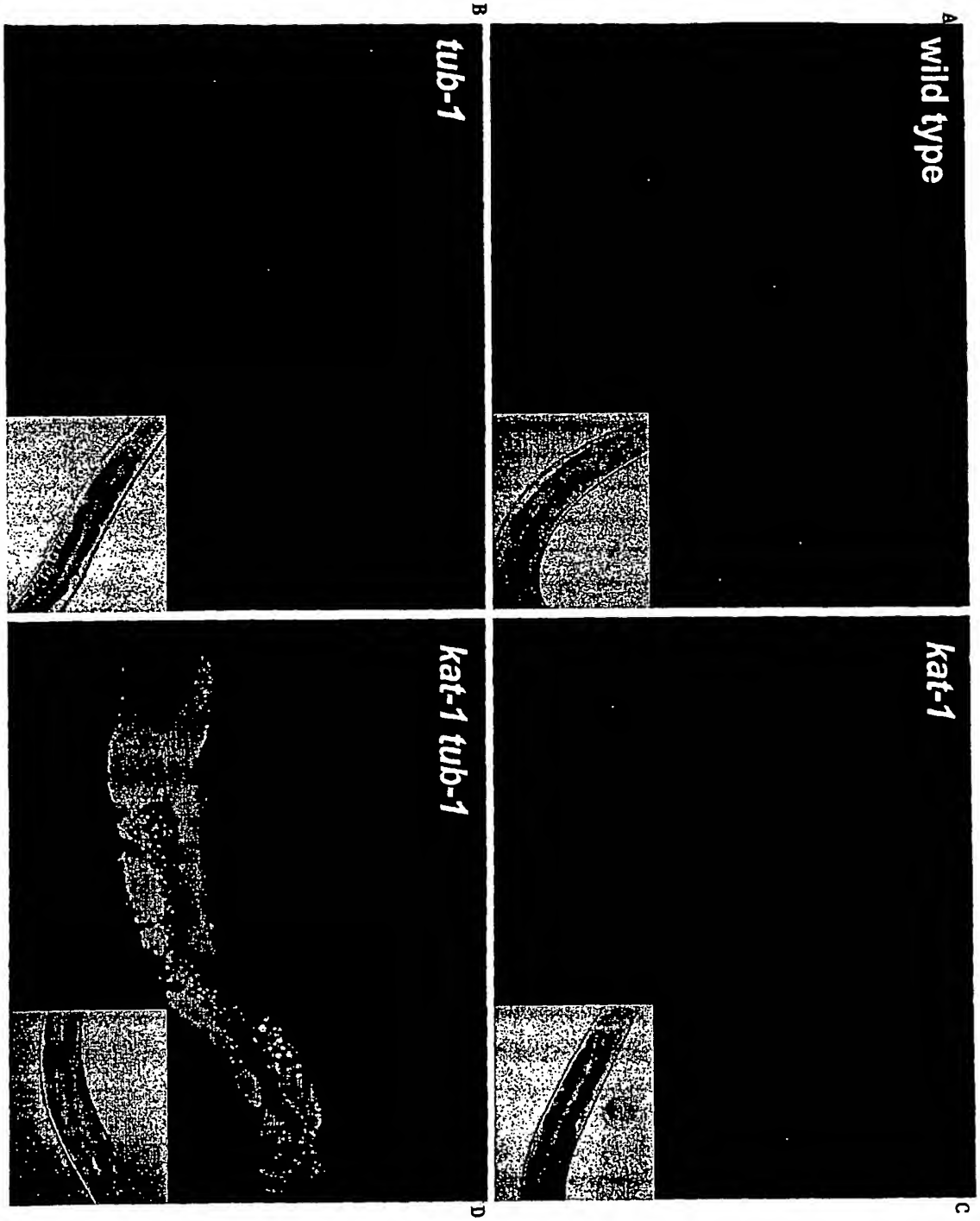


Figure 11

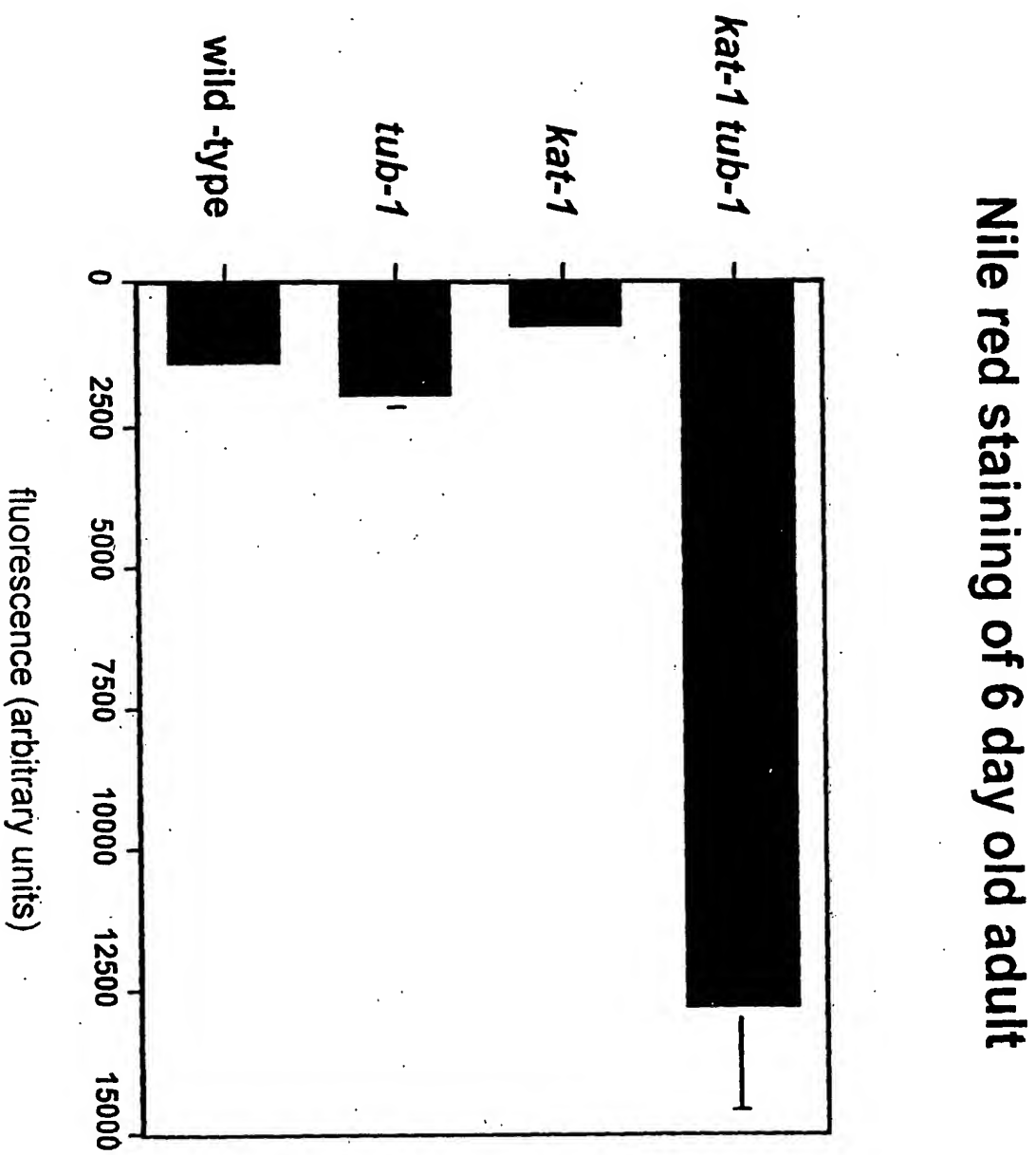

Nile red staining of 6 day old adult
kat-1 tub-1
kat-1
tub-1
wild -type
0
2500
5000
7500
10000
12500
15000
fluorescence (arbitrary units)

Figure 12

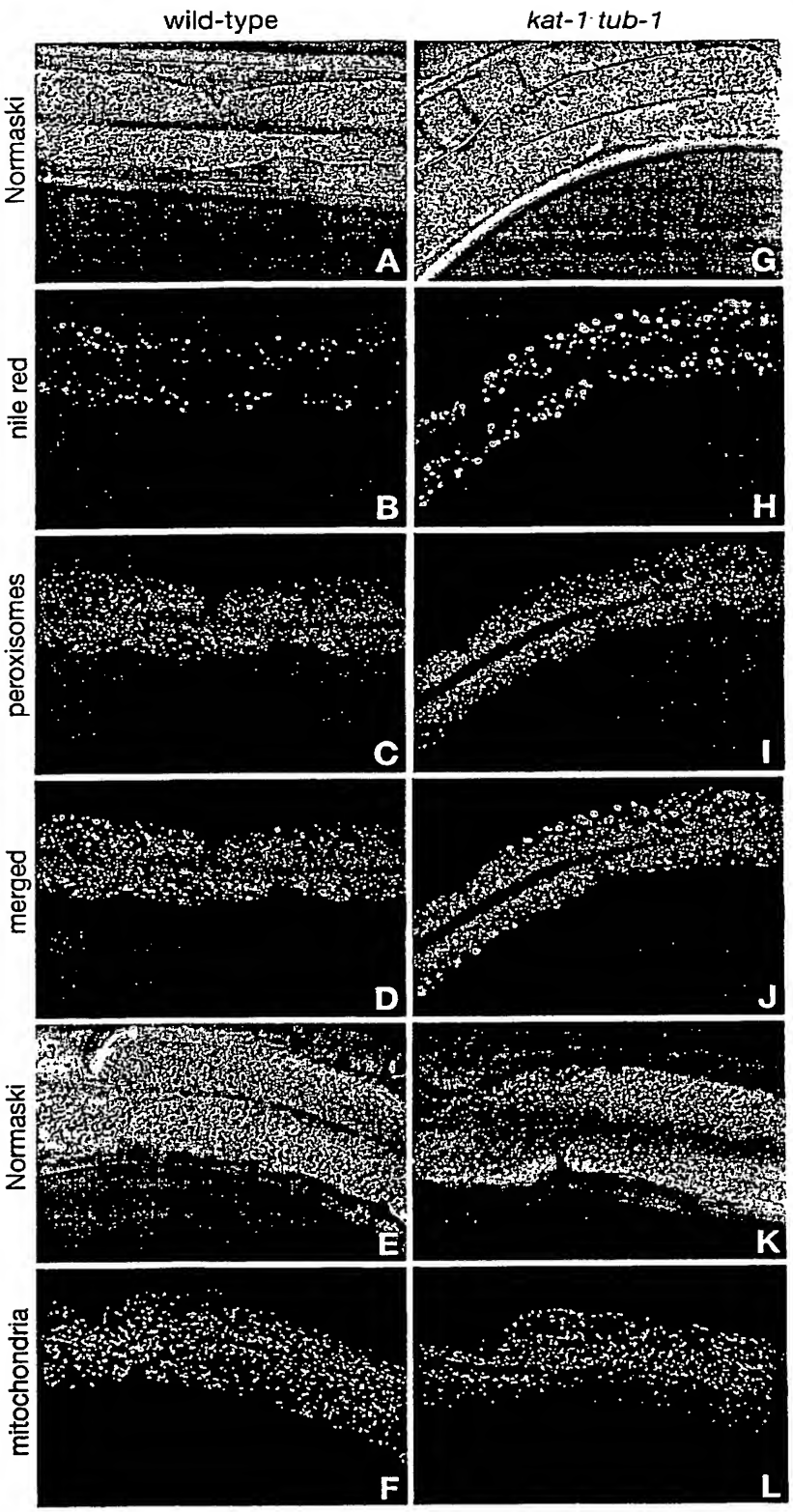
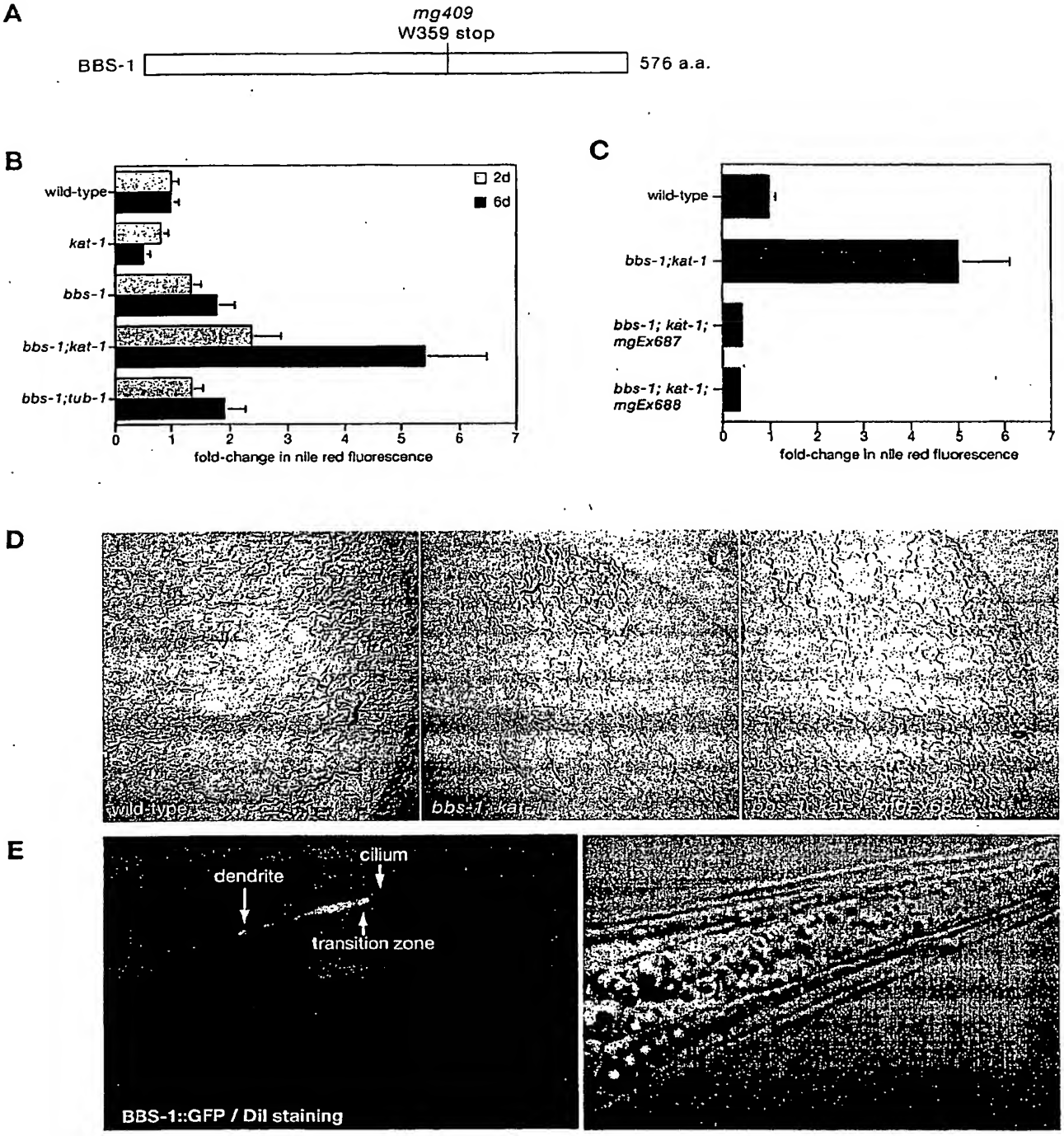

wild-type
kat-1 tub-1
Normaski
nile red
peroxisomes
merged
Normaski
mitochondria
A
G
B
H
C
I
D
J
E
K
F
L

Figure 13A–13E



Alignment of BBS-1 and its human orthologue

Figure 13F

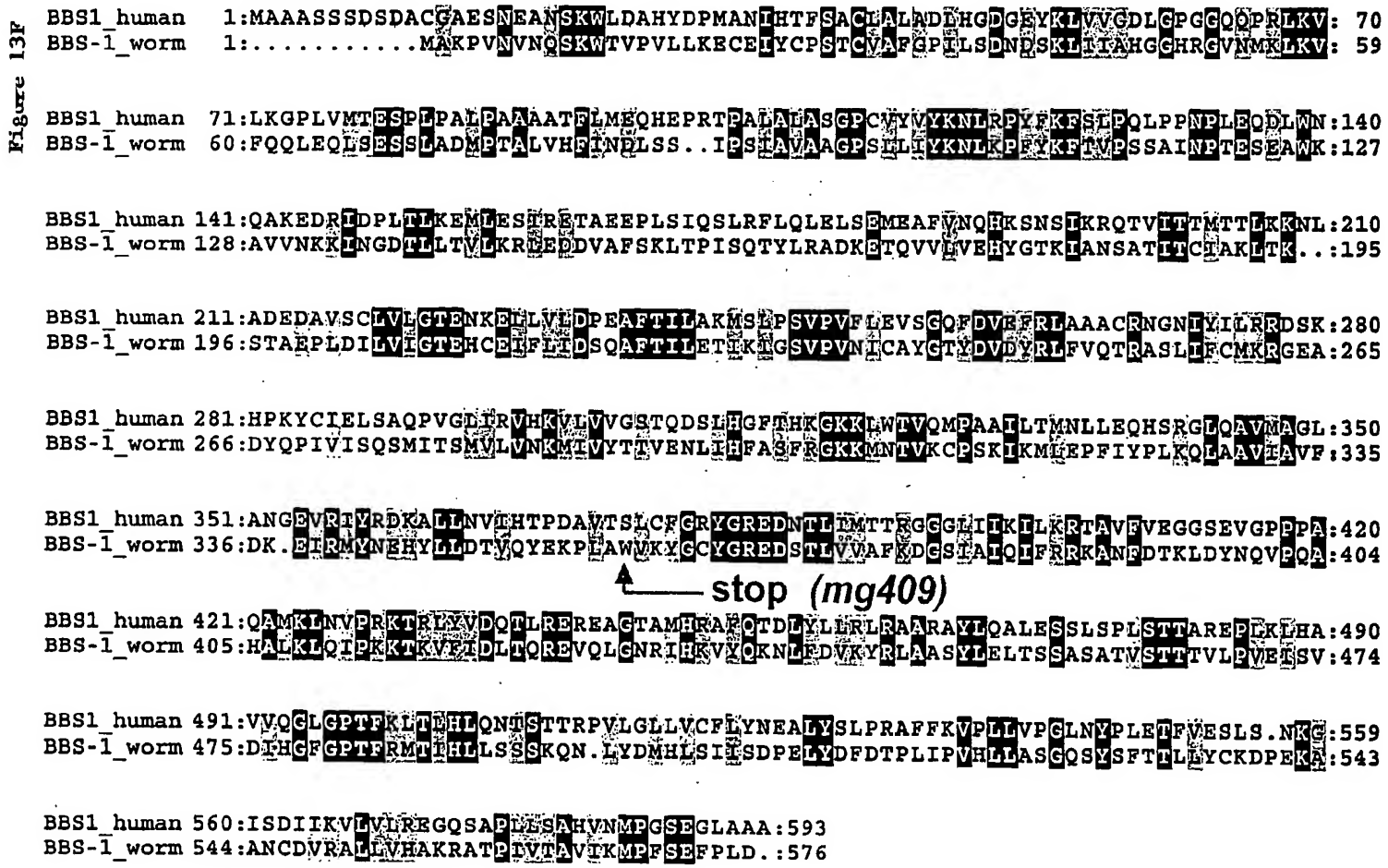
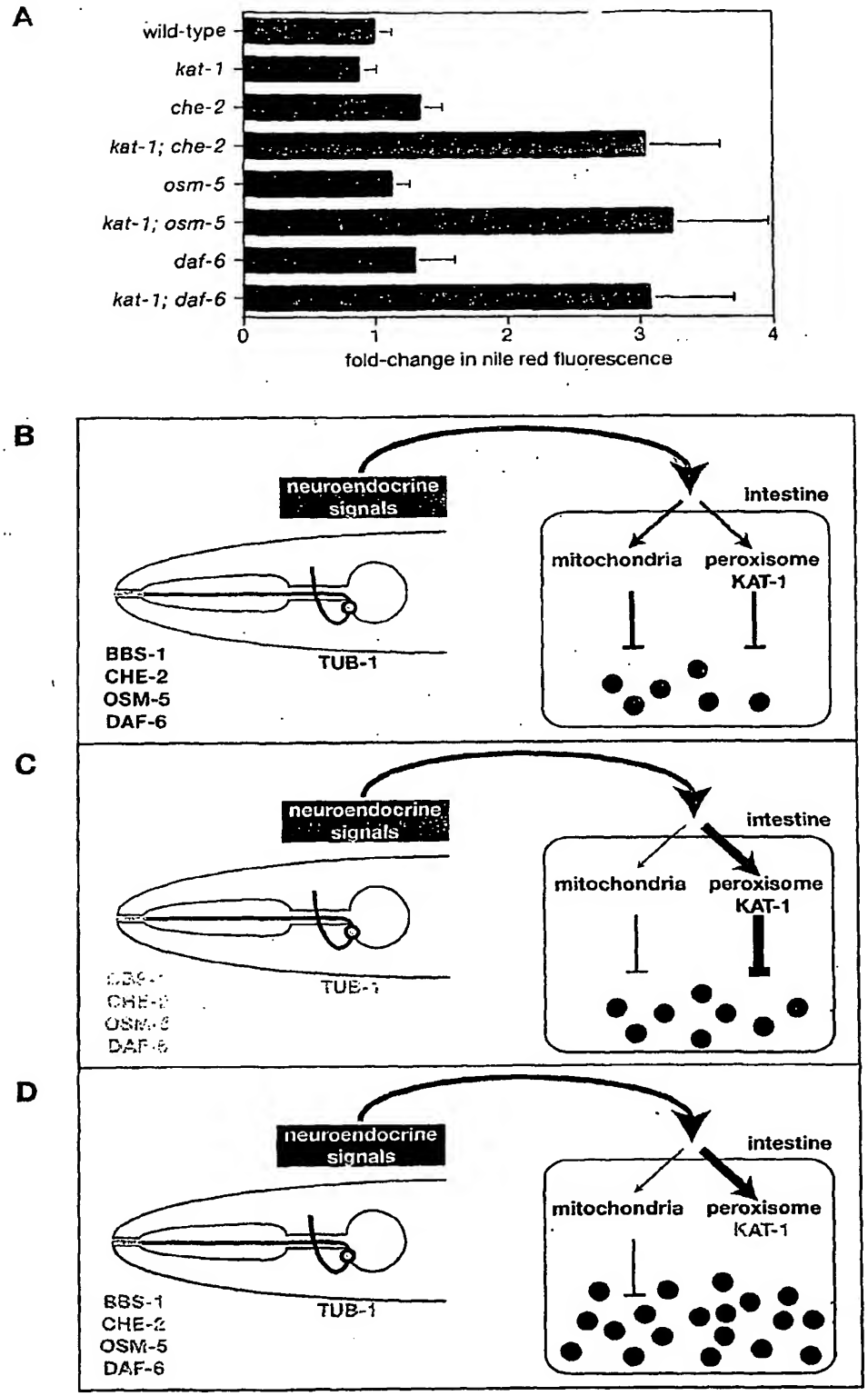


Figure 14A-14D



Synergistic increase in lipid accumulation in *kat-1; che-2*

6-day old adult; 20°C

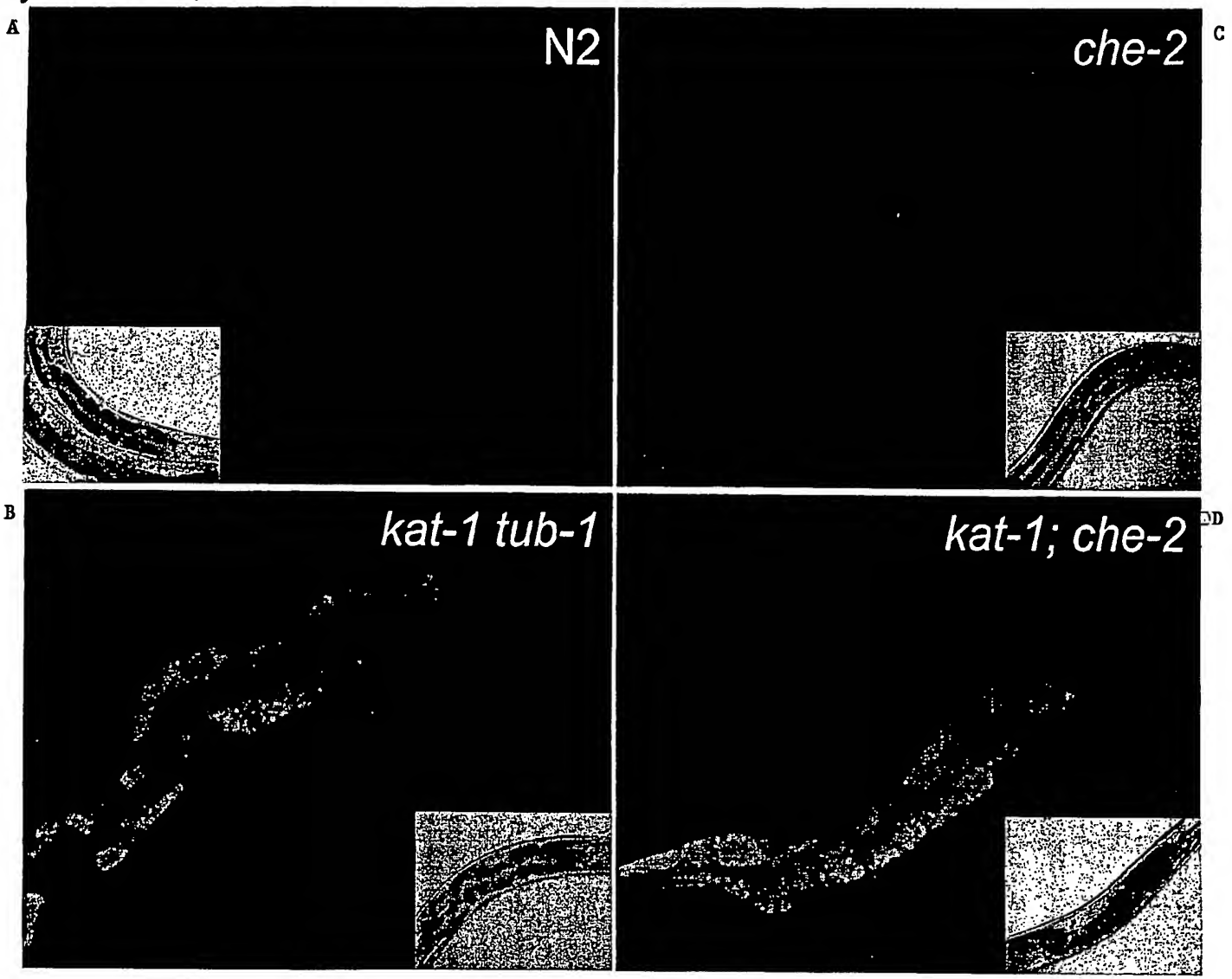


Figure 15A–15D

Molecular lesion of *egl-4(mg410)* in mut17.3

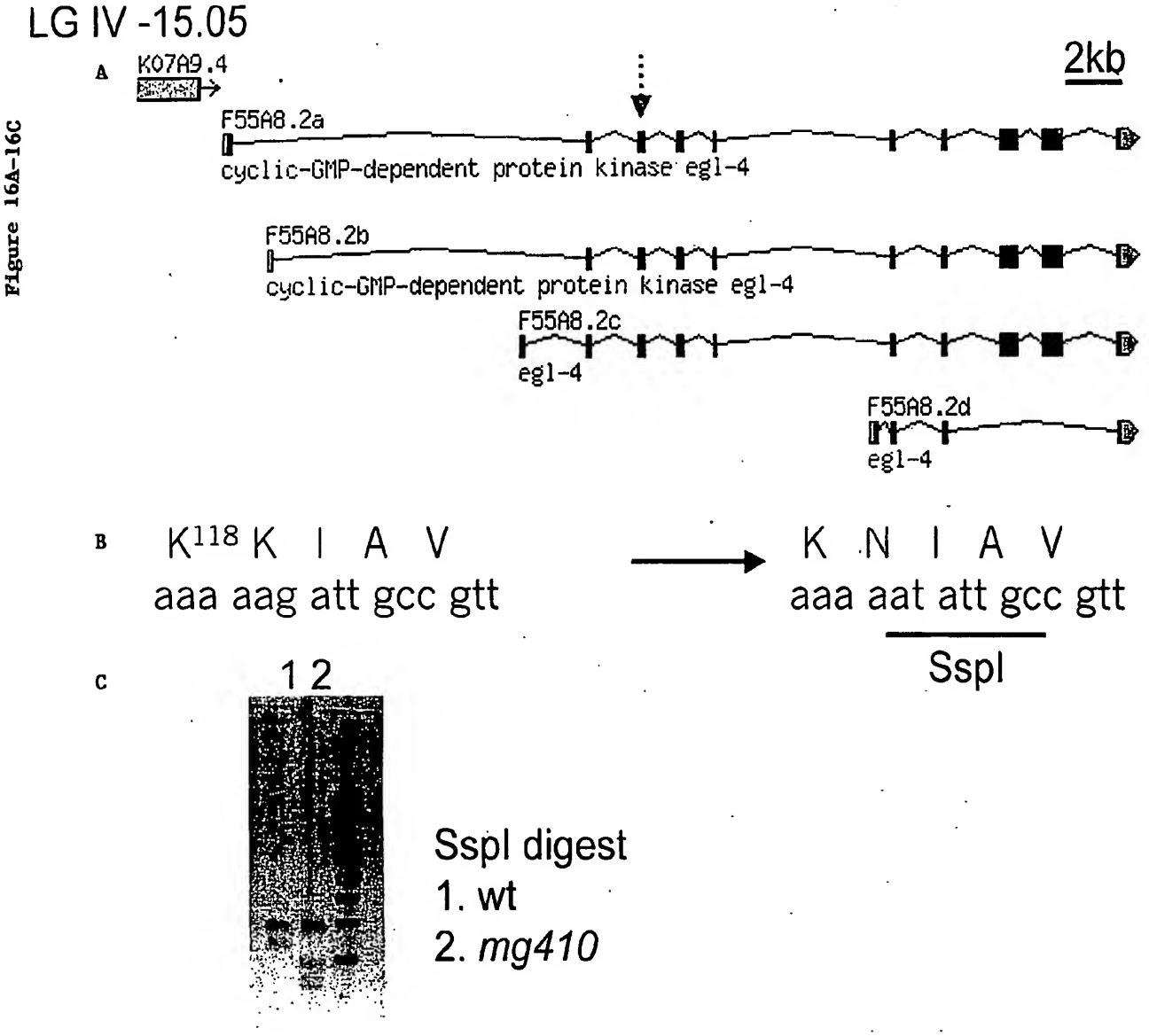
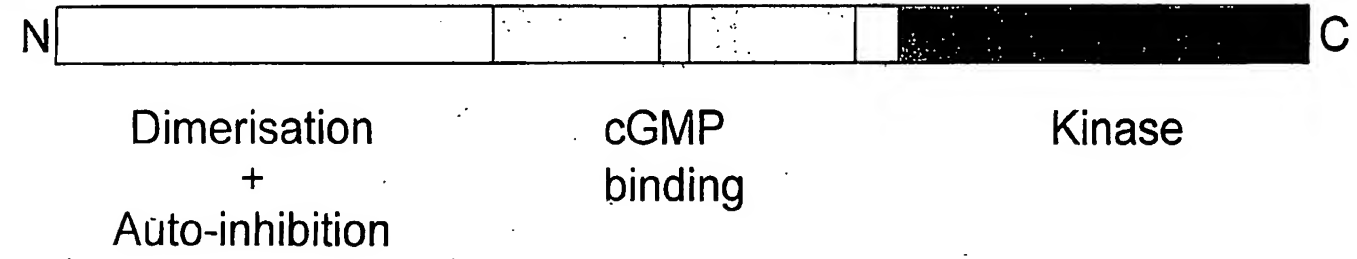


Figure 16A-16C

A dominant mutation in *egl-4* causes excessive lipid accumulation in *mg410*

A

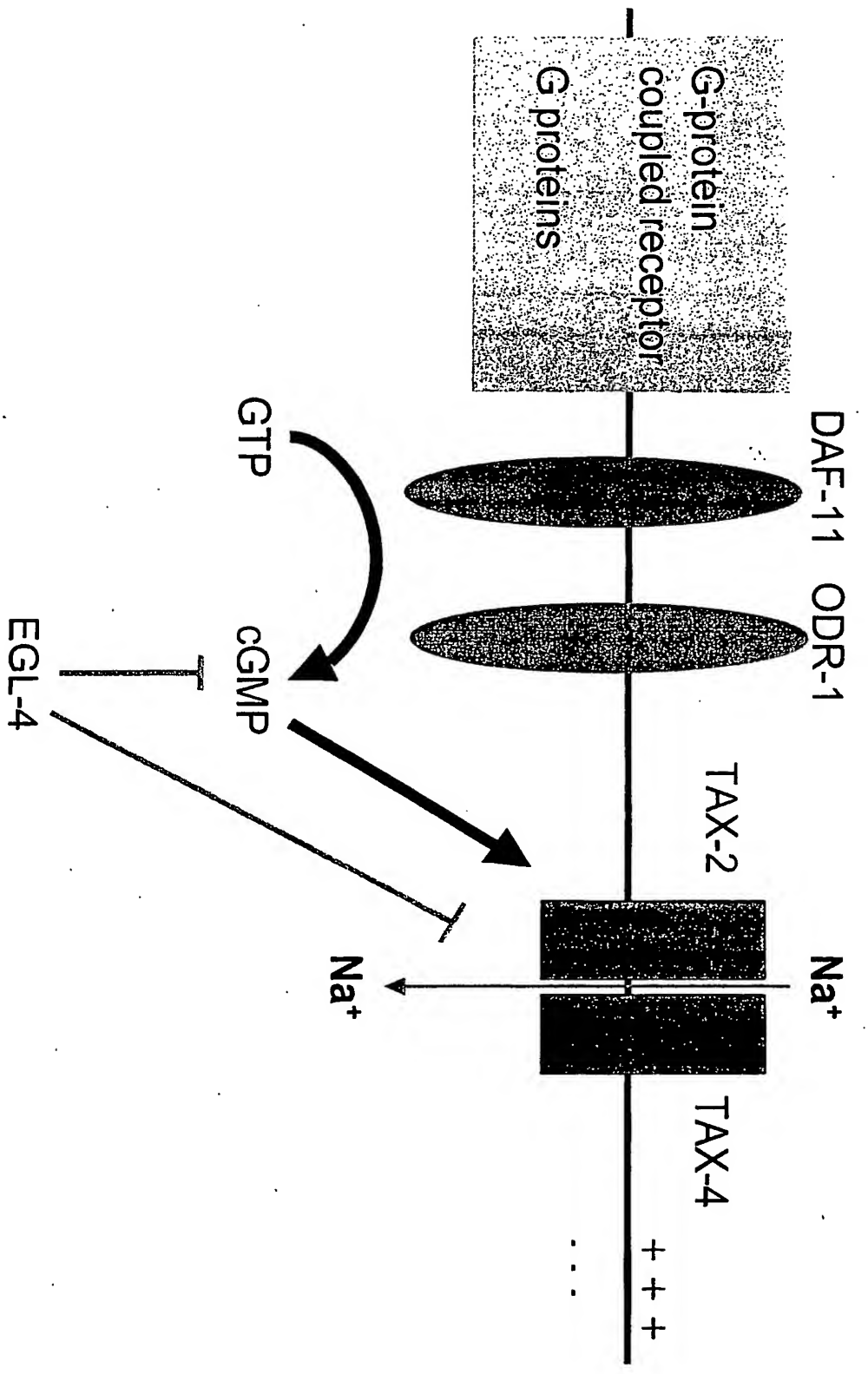


B Kinase substrate motif (K/R)(K/R)X(S/T)X
Pseudo-substrate motif (K/R)(K/R)X A X

C

EGL-4	K	K	I	A	V
EGL-4 (*mg410*)	K	N	I	A	V

Figure 18


G-protein
coupled receptor
G proteins
DAF-11
ODR-1
GTP
cGMP
EGL-4
TAX-2
Na+
Na+
TAX-4
+ + +
. . .

Alignment of EGL-4 and its human orthologue

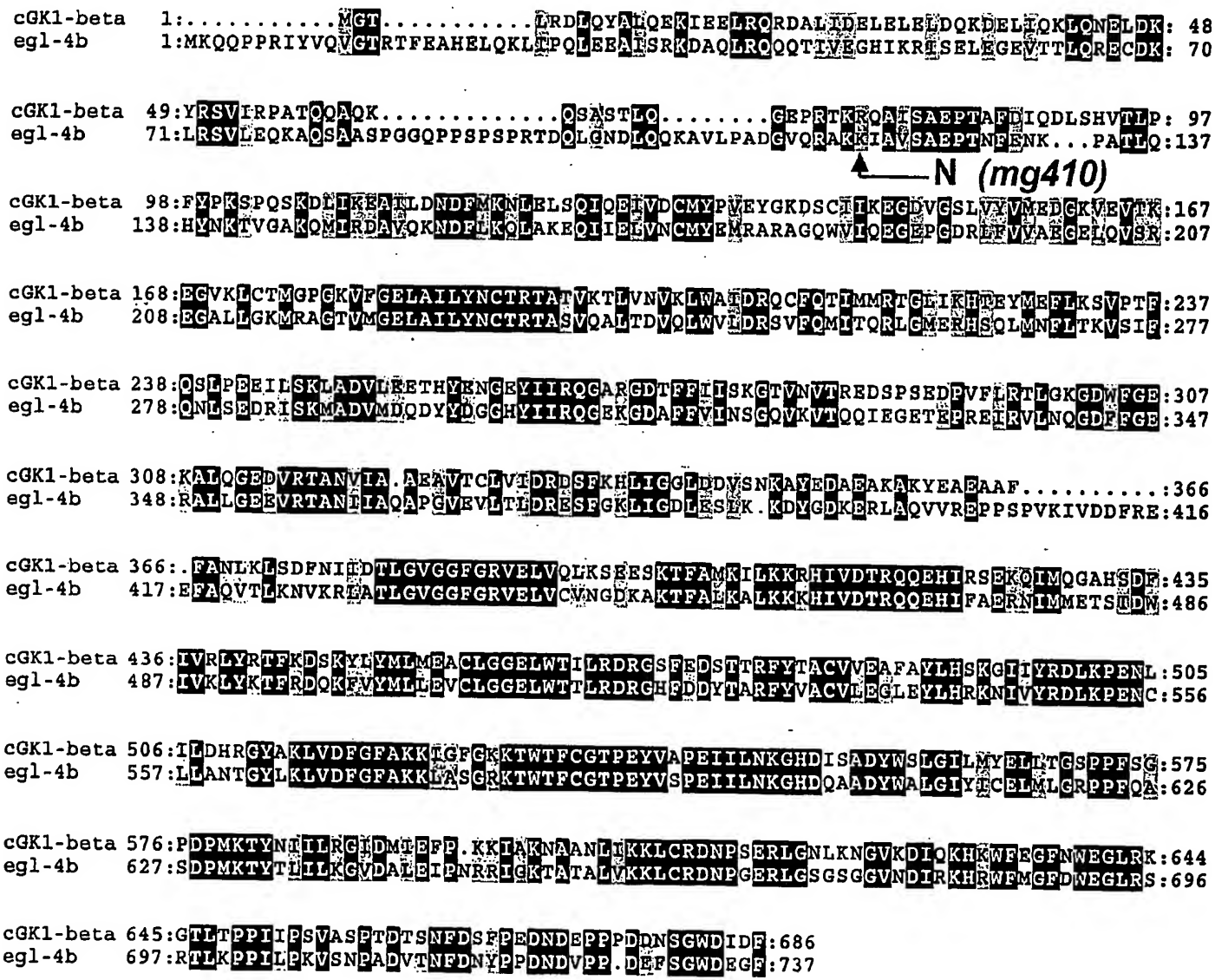


Figure 19

Figure 20

egl-4(lf) suppresses lipid accumulation of kat-1 tub-1 mutant animals
wild-type
6-day old adult animals
20°C
kat-1 tub-1
kat-1 tub-1; egl-4

Figure 21

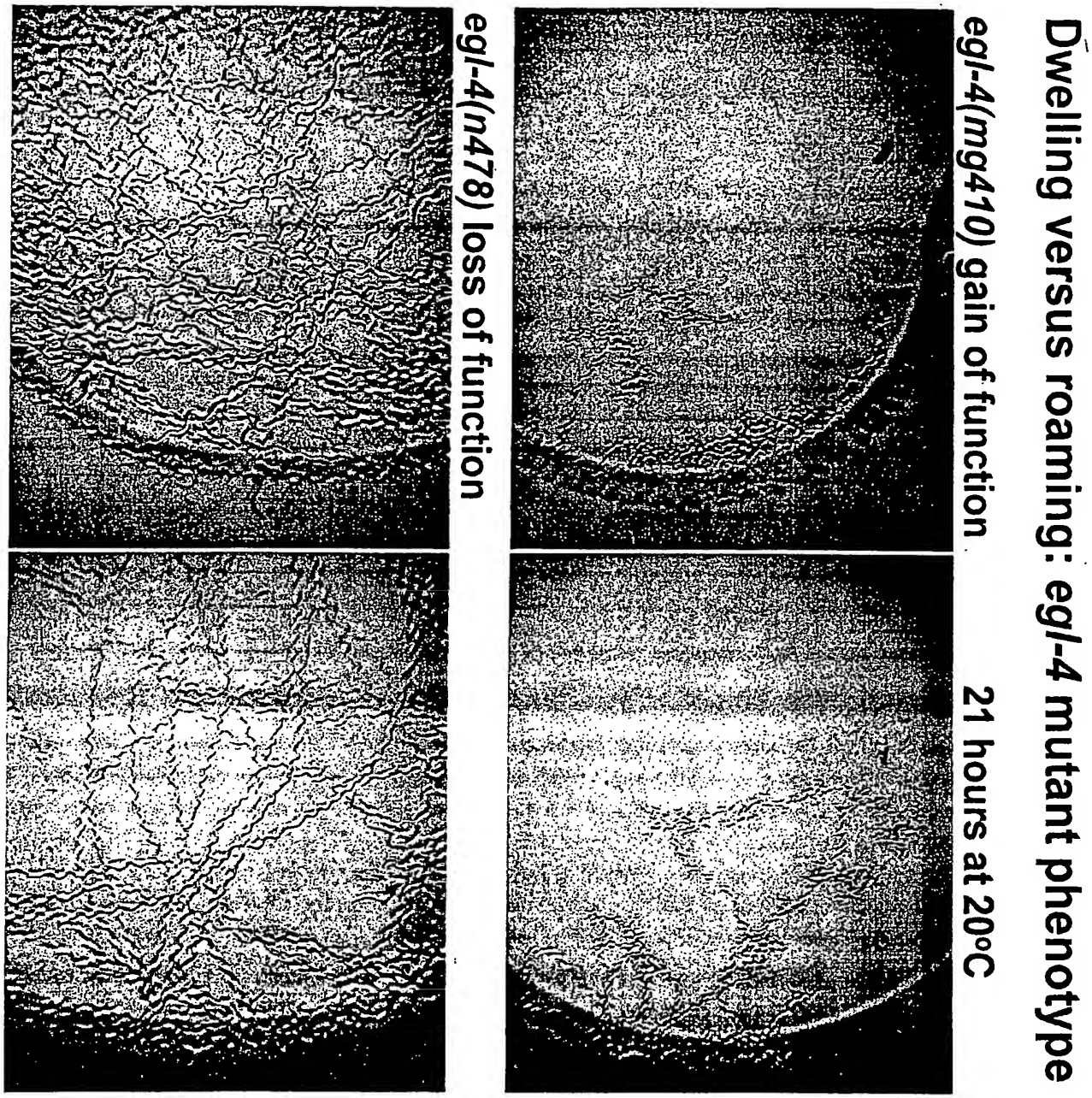

Dwelling versus roaming: egl-4 mutant phenotype
egl-4(mg410) gain of function
21 hours at 20°C
egl-4(n478) loss of function

Figure 22

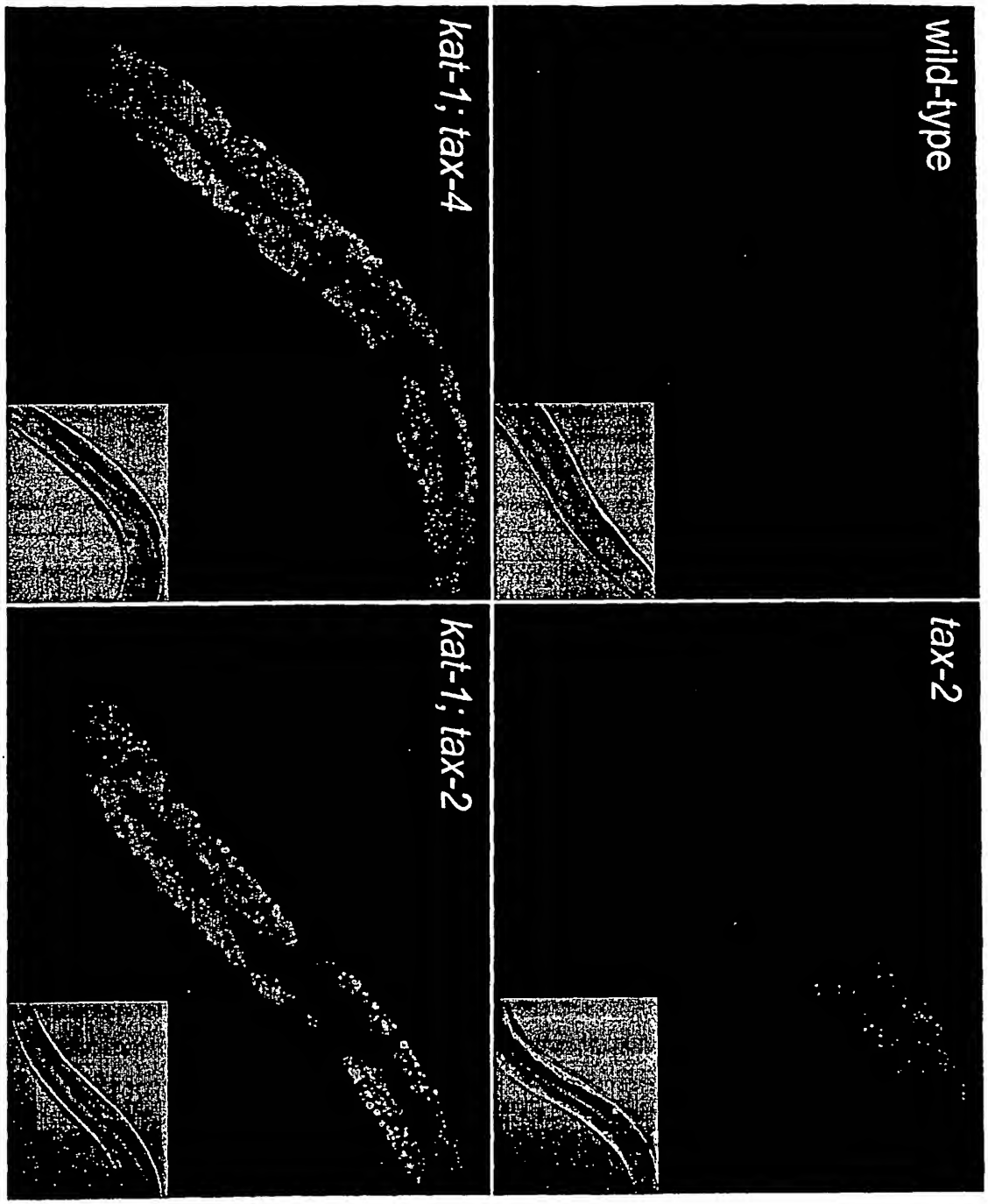

kat-1 enhaces lipid accumulation of tax-2 and tax-4 mutant animals
TAX-2, TAX-4: cGMP gated ion channel
wild-type
tax-2
kat-1; tax-4
kat-1; tax-2

Figure 23

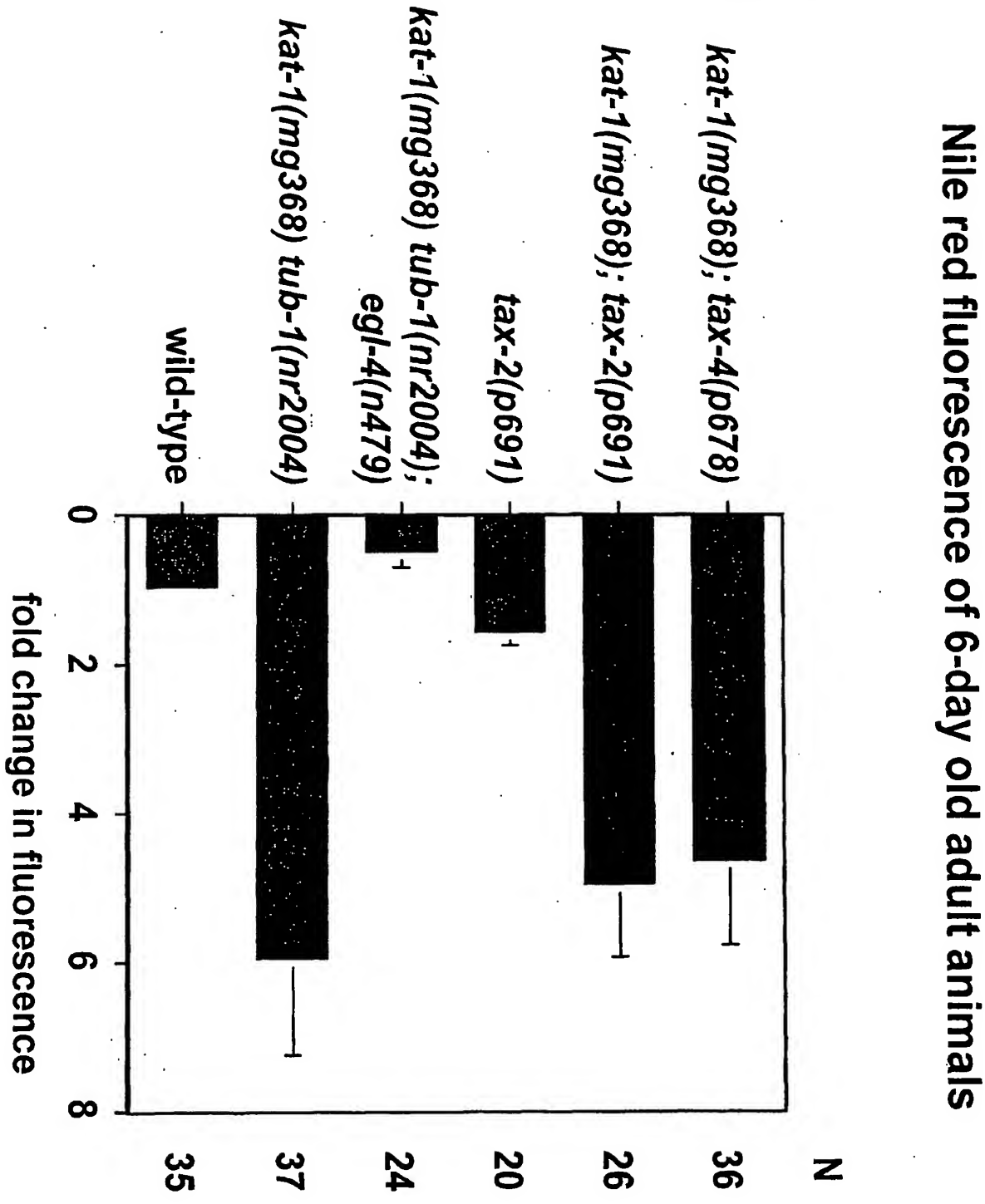

Nile red fluorescence of 6-day old adult animals
kat-1(mg368); tax-4(p678)
kat-1(mg368); tax-2(p691)
tax-2(p691)
kat-1(mg368) tub-1(nr2004); egl-4(n479)
kat-1(mg368) tub-1(nr2004)
wild-type
N
36
26
20
24
37
35
0
2
4
6
8
fold change in fluorescence

Figure 24A–24D

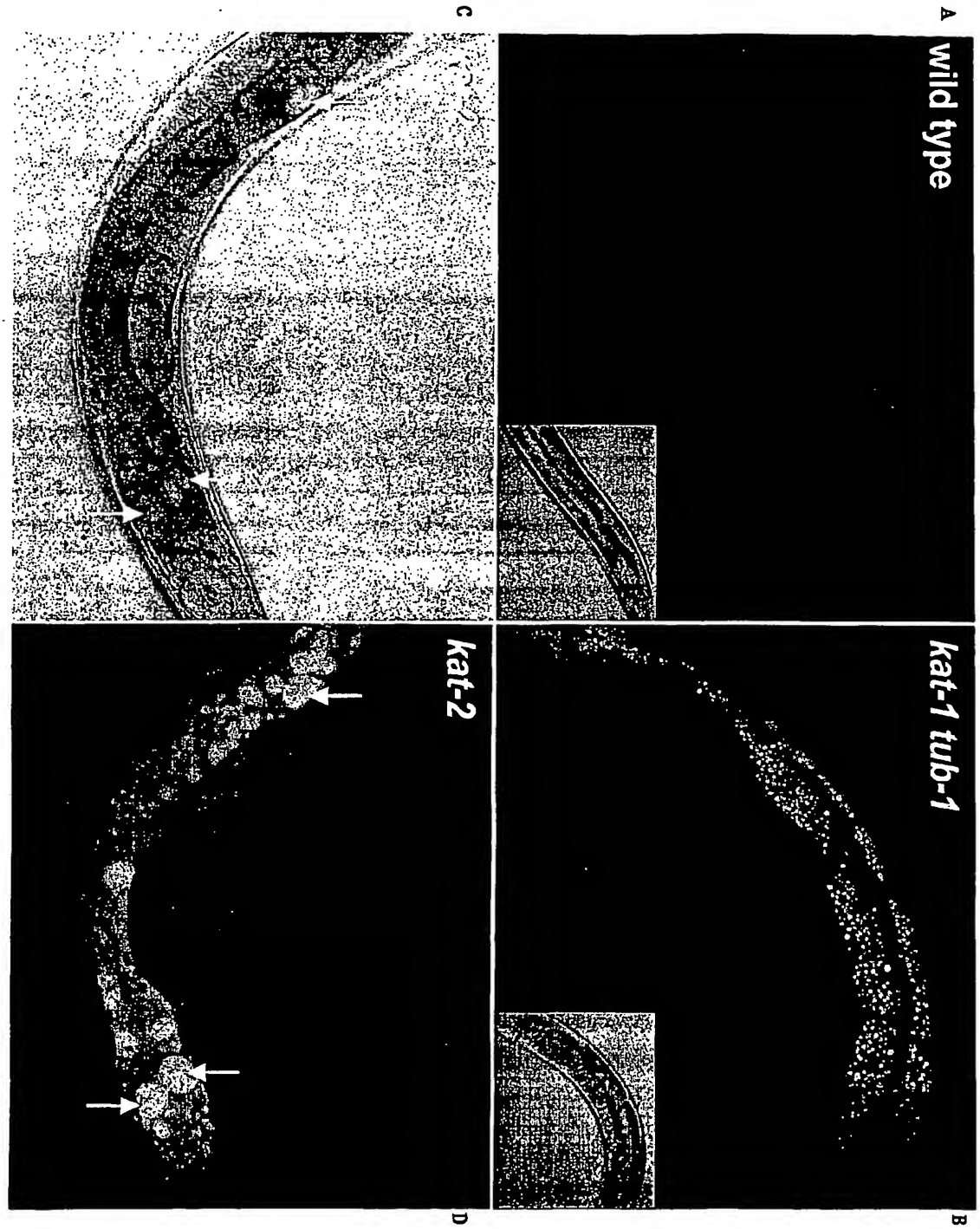
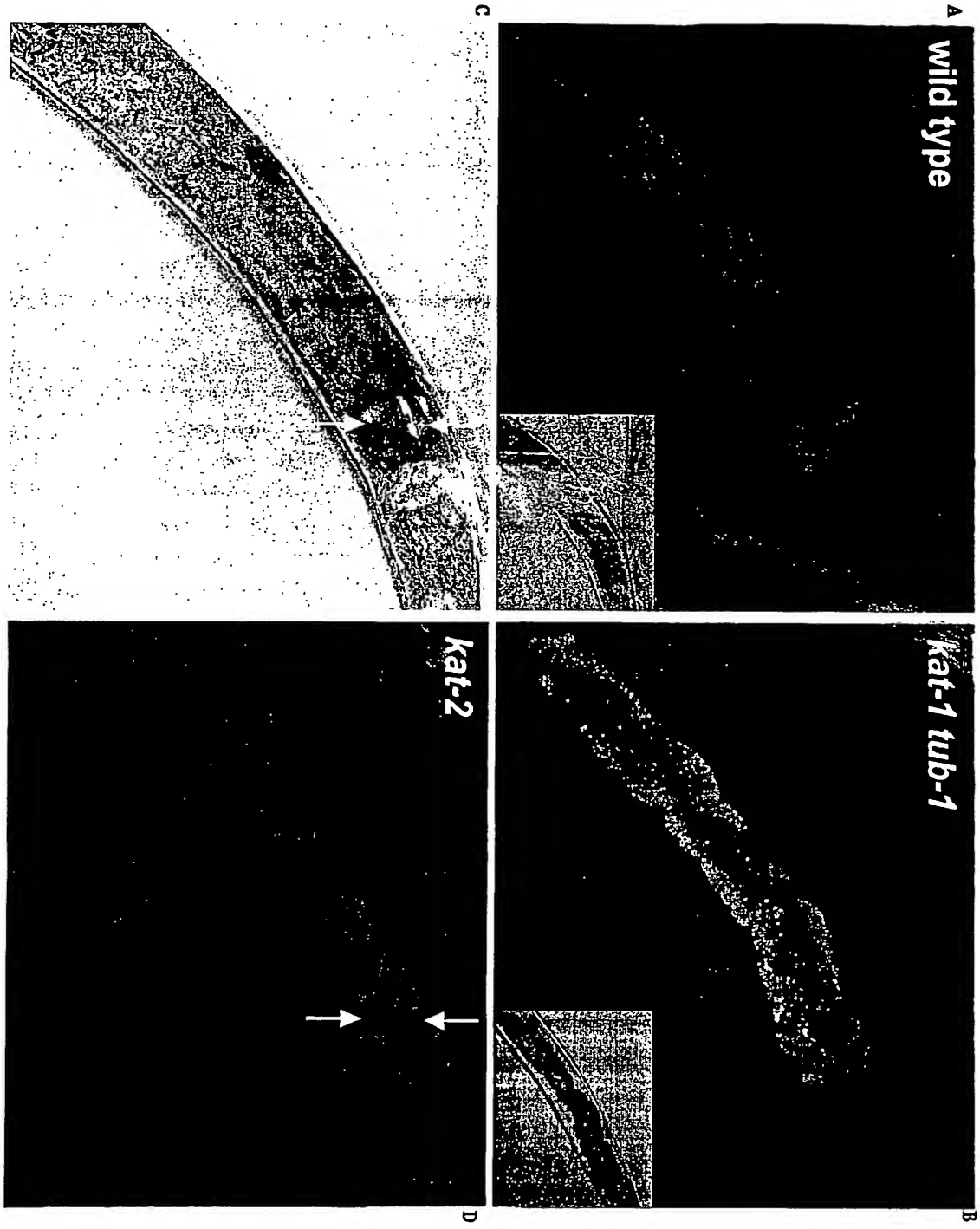


Figure 25A-25D



Nile red staining of 6 day old adult

Figure 26A–26D

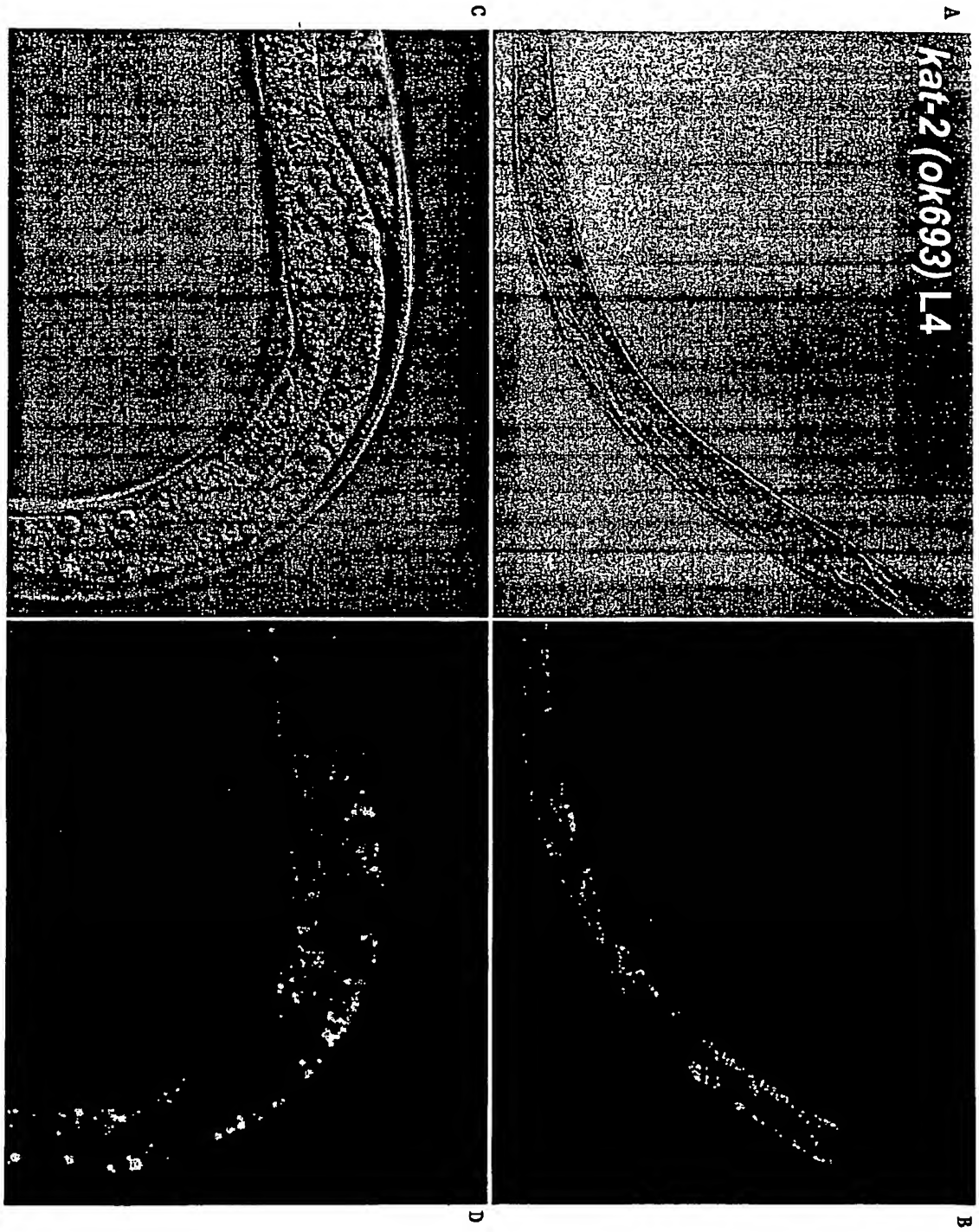


Figure 27